355. "Predicting the future": the impact of reference values on a range of respiratory parameters

P3198

All-age multi-ethnic reference values for spirometry: The global lung function initiative (GLI)

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Background: The GLI (an ERS Task Force) was established to develop the first global reference equations for spirometry. These are the result of unprecedented international cooperation and are endorsed by six international respiratory societies, including the ERS.
Methods: Data from 74,187 healthy non-smokers aged 3-95 years were used to derive reference equations using modern statistical methods, including development of age dependent lower limits of normal.
Results: All-age reference equations are now available for Caucasians, African Americans, South East Asians (south of the Huaihe River and Qinling Mountains), and North East Asians (north of the Huaihe River and Qinling Mountains). For individuals not represented by these four groups a composite equation is provided. Since the observed ethnic differences were proportional to Caucasians, for groups not represented, samples of healthy subjects, composed of at least 300 individuals, studied according to international standards (Quanjer et al ERJ 2011, 37; 658-664) and with height and age measured accurately to one decimal place (Quanjer et al, ERJ 2012, PM:22183491), can be used to validate the GLI and/or create an appropriate adjustment factor (www.lungfunction.org).
Conclusions: The GLI 2012 reference equations are a major step forward and provide a robust reference standard to streamline interpretation of spirometry across all-ages worldwide. Widespread use of the GLI equations will, however, depend on timely implementation by manufacturers of spirometric devices.

P3199

A comparative study of FVC, FEV_1, and TLC in non-smoking Saudi students at Eastern Province, Saudi Arabia with Caucasian reference values

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Introduction: It is well-known that pulmonary function testing (PFT) values vary with height, age, gender, and ethnicity.[1] The influence of ethnic variation on PFT in particular has been the topic of numerous studies conducted globally.[1,2] In Saudi Arabia (SA), the currently available reference values (RV) for PFT are based on data from the Caucasian population. We aimed to compare Saudi measured values,

for forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and total lung capacity (TLC), with Caucasian RV.
Methods: Healthy non-smoker university students were recruited to perform spirometry and plethysmography. Measurements were obtained according to ATS/ERS recommendations, standardized for height and age and compared with Caucasian RV.
Results: We studied 128 subjects, 16 of which were excluded for technical reasons. Significant difference ($p<0.01$) was found between the measured values in Saudis (52 males and 60 females) and Caucasian RV. The means for the measured values of FVC, FEV_1 and TLC for Saudis were found to be lower than the means of RV for Caucasians by about 10%, 5% and 8% respectively for males and 16%, 12% and 5% respectively for females.
Discussion: Matching the reference and patient populations when selecting RV for PFT is significant.[3] The observed differences we found between Saudi's PF and Caucasian RV can be deemed of great importance and maybe explained in terms of environmental and life-style factors. However, larger study is required to confirm these findings.
References:
[1] Hankinson et al. 1999 AJRCCM; 159:179-187
[2] Al-Riyami et al. 2004 Respirology; 9:387-391
[3] Wanger et al. 2005 ERJ; 26:511-522.

P3200
Reference values for spirometry in healthy subjects 17 to 25 years
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Background: Spirometry is the most common way to evaluate pulmonary function. The European Respiratory Society recommends the development of new reference equations, in order to upgrade and improve the existing ones.
Aim: Develop reference equations to calculate reference values adjusted to a healthy population of college students.
Methods: A total of 49 healthy female individuals with ages ranging 17 to 25 years old were enrolled in the present study. A standardized respiratory and allergy symptoms questionnaire was applied and spirometry was performed in the selected individuals. FEV1, FVC and FEV1/FVC were used as dependent variables in simple and multivariate linear regression models.
Results: Height is the variable that best explains variation of FEV1 ($r2 = 0.36$; $p < 0.001$) and FVC ($r2 = 0.44$; $p < 0.001$), while weight is the variable that best explains FEV1/FVC ($r2 = 0.15$; $p = 0.006$). Knudson's equations were the most different from this model, while Quanjer's were the closest.
Conclusions: We've calculated new reference equations for healthy individuals, with ages ranging from 17 to 25 years old. The results highlight the need for the use of appropriate reference equations, taking into consideration the individual characteristics of the target population.

P3201
Spirometry measurements in the morbid obesity
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Background: The obesity is a particular case of thoracic respiratory function restriction. Obstructive Apnea Syndrome and hypoventilation have been described in relationship to the morbid obesity (MO).
Objective: To evaluate the alterations presented in spirometric measurements concerning the healthy subject with morbid obesity.
Methods: Spirometry and flow-volume curve were performed in 44 patients suffering of MO studied in our Departament. Of 44 cases, 8 were male (18.2%) with a mean age of 37±8.8 years and 36 women (81.8%) with a mean age of 39.9±11.1 years.

Table 1. Physical attributes

	Male		Women	
	Mean	S.D.	Mean	S.D.
Age	37	8.8	39.9	11.1
Weight (kg)	135.5	8.7	122.6	18.2
Height (cm)	171.8	4.8	157.5	7.0
BMI*	46	4.3	49.7	7.5

*Body Mass Index.

Table 2. Spirometry results

	Male		Women	
	Mean	S.D.	Mean	S.D.
FEV1 (% pred.)	86.7	22.9	88	17.5
FVC (% pred.)	88.2	20.9	89.8	17.7
FEV1/FVC	87.3	16.4	84.4	6.3
REF (% pred.)	72.1	22.7	85.5	20.5
FEV (% pred.)	86.2	36.4	80.3	28.3

Conclusions: There are no spirometry alterations in patients with morbid obesity with no history of cardiovascular, skeletal, neuromuscular or respiratory diseases.There are no difference between sexes.

P3202
Comparison of different predicted and lower limit of normal (LLN) values in ventilation disorders detection
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Aim: To estimate the agreement of Russian equations (Klement), ECCS and NhanesIII spirometry evaluating systems in determining the types of ventilation abnormalities by predicted and LLN (5th percentile) values.
Materials and methods: The study enrolled 7,779 Caucasians examined in pulmonary clinics of St.Petersburg Pavlov's State Medical University in 2005-2011: 3,584 males (mean age 47.40±0.25, mean height 175.44±0.18) and 4,195 females (mean age 49.66±0.20, mean height 162.29±0.10). The cases that can not be classified as norm, obstruction or restriction, were accumulated in the "mixed" group.
Conclusion: The best agreement was obtained by ECCS and Klement systems both in predicted values and LLN. NhanesIII significantly differs from both Klement and ECCS in LLN for all groups. In predicted values these three systems agreed in obstruction but still generally disagree in norm and restriction.

P3203
The effect of body composition on pulmonary function
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Background: The pulmonary function test (PFT) is the most basic test methods to diagnosis lung disease. The purpose of this study was to research correlation of the body mass index (BMI), the fat percentage of the body mass (Fat%), the muscle mass, the fat-free mass (FFM) and the fat-free mass index (FFMI), waist-hip ratio (WHR) on the forced expiratory volume curve.

Abstract P3202 – Table 1

	Klement (1)	ECCS (2)	NHANES III (3)	Cohen's kappa		
				1-2	2-3	1-3
Norm: FEV1/FVC ≥0.7; FVC >80%Pred; FVC ≥LLN						
FEV1 >80%Pred	2978 (0.38)	3146 (0.40)	2383 (0.31)	0.85 (0.83–0.87)	0.66 (0.64–0.68)	0.74 (0.73–0.76)
FEV1 ≥LLN	3586 (0.46)	3415 (0.44)	2301 (0.30)	0.86 (0.85–0.88)	0.52 (0.50–0.54)	0.46 (0.44–0.48)
Obstruction: FEV1/FVC <0.7						
FEV1 ≤80%Pred	2765 (0.36)	2710 (0.35)	2855 (0.37)	0.87 (0.84–0.90)	0.74 (0.70–0.78)	0.82 (0.78–0.85)
FEV1 <LLN	2506 (0.32)	2508 (0.32)	2836 (0.36)	0.91 (0.90–0.93)	0.55 (0.51–0.59)	0.55 (0.51–0.59)
Restriction: FEV1/FVC ≥0.7						
FVC ≤80%Pred	1247 (0.16)	1089 (0.14)	2035 (0.26)	0.85 (0.83–0.87)	0.56 (0.54–0.58)	0.64 (0.62–0.66)
FVC <LLN	784 (0.10)	921 (0.12)	2160 (0.28)	0.87 (0.85–0.89)	0.44 (0.42–0.46)	0.38 (0.36–0.40)
Mixed						
%Pred	789 (0.10)	834 (0.11)	506 (0.06)			
LLN	903 (0.12)	935 (0.12)	482 (0.06)			

Method: Between March and April 2009, a total of 291 subjects were enrolled. 152 men and 139 female (mean age: 46.3±9.92) were measured the FVC, FEV_1, FEF_{25-75} from the forced expiratory volume curve by the spirometry and the body composition by the bioelectrical impedance method. Correlation and multiple linear regression between body composition and pulmonary function were used executed.
Result: BMI and Fat% had no correlation with FVC, FEV_1 in male, but FFMI is positively correlation. In contrast, BMI and Fat% had correlation with FVC, FEV_1 in female, but FFMI had no correlation. Both male and female, FVC and FEV_1 had negatively correlation with WHR (male FVC r=-0.327, FEV_1 r=-0.36; p-value<0.05) (female FVC r=-0.175, FEV_1 r=-0.213; p-value<0.05).
In a multiple linear regression of considering body composition at total sex group, FVC was explained FFM, BMI, FFMI in order (R^2=0.579, 0.657, 0.663), FEV_1 was explained only Fat% (R^2=0.011), FEF_{25-75} was explained muscle mass, FFMI, FFM (R^2=0.126, 0.138, 0.148).
Conclusion: The BMI, Fat%, muscle mass, FFM, FFMI, WHR have significant association with pulmonary function but R^2 (coefficient of determination) were not high enough for explaining lung function.

P3204
Reference values for exhaled breath temperature in healthy subjects aged 17 to 25 years old
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Background: Exhaled Breath Temperature (EBT) is a potential new method for diagnosis and management of respiratory diseases. However, there are few studies showing determinant factors or reference values.
Aim: Establish reference equations for EBT.
Methods: A total of 984 standardized respiratory and allergy symptoms questionnaire questionnaires, were distributed and collected, allowing the selection of 50 healthy subjects, which carried out tests of EBT. Simple and multivariate linear regression analysis was used to obtain reference equations and for determining the variables that were expected to influence the values.
Results: Height is the model that best explains the variation of EBT (r2=0.25, p<0.001). There was a weak but significant correlation between EBT and FVC (r=0.3, p=0.036). There was no significant difference between the values obtained in healthy individuals compared to other studies, but there was a significant difference when compared to asthmatic subjects.
Conclusions: EBT is affected by height, which can also be related to lung volumes. Defining reference equations may help explore the potential of EBT as a simple, inexpensive and easily applied biomarker in clinical practice.

P3205
Forced oscillation technique (FOT) reference values: Does one size fit all?
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Introduction: International reference ranges have been produced for spirometry. In comparison, current FOT reference values are limited to specific equipment and populations. We aimed to determine whether current reference values created from Australian and Italian children were applicable for Mexican children.
Methods: Respiratory resistance (Rrs) and reactance (Xrs) were measured using FOT (Cosmed,Italy) in 585 children (292 males) 3-5 years old as part of a birth cohort in Mexico. Regression analysis determined factors predicting Rrs and Xrs at 6 and 8Hz and Zscores calculated. Calogero compared regression equations created in Italian children (3-6 years) to Australian children (4-6 years),with no significant difference reported in Rrs8 (p=0.43) and minor differences, which were within test variability, in Xrs8 (p=0.012). Based on this, Australian reference values were used for comparison. Zscores were calculated for the Mexican group using the derived regression equation. Zscores were also calculated for the Mexican group using the Australian reference values and the differences in these Zscores were compared using a paired t test.
Results: Height was a significant predictor of Rrs and Xrs (p<0.05), but gender, age and weight were not (p>0.05). The Australian reference equation overestimated lung function in Mexican children (paired t-test) for Rrs and Xrs at 6 and 8Hz compared to data created using the Mexican equation (p<0.001).
Conclusions: Despite similarities between current Australian and Italian FOT reference values these reference values are not valid for use in Mexican children aged 3-5 years. This highlights that one reference set from different parts of the world is not advisable for use in FOT.

P3206
Impact of a pulmonary laboratory quality control oversight on continual improvement
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Introduction: The purpose of this study was to evaluate the impact of a quality control (QC) oversight program on compliance with QC, biological coefficient of variation (CV) targets, and test performance improvements.
Methods: The Diagnostic Accreditation Program (DAP) of British Columbia is responsible for accrediting 27 pulmonary function (PF) laboratories representing 45 testing systems throughout the Canadian province. In 2008 DAP elevated the required elements of their quality assurance program to be more consistent with the current ATS-ERS recommendations for QC testing. This included increasing the frequency of the biological testing and adding a diffusing capacity mechanical QC model. DAP also changed the data review model to include assessment by an external consultant with a feedback report process to the sites. We compared the data through 2011 to assess the impact of the feedback process. Data were categorized into major and minor subsets for compliance, BioQC targets, and test performance based on an assessment of overall impact of the deficiency on lab performance (e.g. BioQC DLCO CV target < 5%, a CV >5<10 categorized as minor; CV >10% a major deficiency).
Results:

Category of Deficiency	Submission Cycle 05 (2008)	Submission Cycle 10 (2011)	% Improvement
Compliance Major	26	3	88%
Compliance Minor	28	20	29%
BioQC Major	8	2	75%
BioQC Minor	23	7	70%
Test performance	10	5	50%
Total	95	37	61% P<0.05

Discussion: There was a significant improvement in all three areas of the monitoring program with a total improvement of 61% (p<0.05). Using a formal external oversight process which includes written feedback appears to improve the overall outcome of this regulated quality assurance program.

P3207
Validation of spirometer calibration syringes
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The calibration syringe is probably the most important instrument in pulmonary function laboratories, yet no validation results have been published.
Methods: We weighed a 3 L calibration syringe before and after emptying it of water and determined the corresponding volume of gas by using a modified rolling seal spirometer.
Results: The volume of a spirometer calibration syringe could be verified with an accuracy of ± 15 mL. All syringes larger than one litre had volumes within the label claimed volume ± 0.5%.

Syringe Manufacturer	Volume claimed, ml	Volume verified	Volume deviation, ml (pct.)	Volume SD, ml	Syringe duty cycle
Hans Rudolph	2,989	2,988	1 (0.03)	0.8	1990–1991 & 1998–1999. Epidemiology
Hans Rudolph	5,500	5,530	30 (0.05)	1,7	Never
Hans Rudolph	2,500	2,496	4 (0.2)	4.6	Never
Hans Rudolph	3,000	2,987	13 (0.4)	2.9	Never
Ferraris	3,000	2,988	12 (0.4)	2.9	2002–2005 Clinical trial
Ferraris	3,000	3,002	07 (0.2)	0.9	2002–2005 Clinical trial
Ferraris	3,000	2,990	10 (0.3)	0.7	2002–2005 Clinical trial
Biotrine	3,000	2,994	06 (0.2)	2	1975–1990
Biotrine	3,000	3,002	02 (0.1)	4	2002–2005 Clinical trial
Cardinal	3,000	2,988	12 (0.4)	3	2008–2010
Jaeger	1,000	0,976	24 (2.4)	1	Never
Jaeger	1,000*3	2,952	48 (1.6)	5	Never
Vitalograph	1,000	0,984	16 (1.6)	11	1998–2011 Routine
Vitalograph	1,000*3	2,979	21 (0.7)	15	1998–2011 Routine

All results are based on 10 measurements. One litre syringes were tested at 1 litre and the sum of three strokes. None of the syringes had been serviced by the manufacturer or by a certified company.

Conclusion: Spirometer calibration syringes have a stable stroke volumes. The maximal interval between syringe validations should perhaps be extended beyond the 1-year period required by current standards. Use of two syringes would allow one syringe exceeding the maximal permissible error to be detected earlier.

P3208

The comparison study on the effects of high versus low flux membrane on pulmonary function tests in hemodialysis patients

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Background: Several studies have been carried out to evaluate the effects of dialysis on pulmonary function tests (PFT). Dialysis procedure may reduce volumes and capacities of the lung or cause hypoxia; however, based on our knowledge, there was no previous study on evaluation of effects of membrane type (high flux vs. low flux) on PFT in these patients. The aim of this study was the evaluation of this relationship.
Materials and methods: In a cross-sectional study, 43 hemodialysis patients without pulmonary disease were enrolled. In these patients dialysis were conducted by low and high flux membranes and before and after of procedure, spirometry were done and the results were evaluated by t-test and chi square.
Results: Mean age of the patients was 56.34 years. Twenty three women (53.5%) and 20 men (46.5%) were enrolled. Patients' body weight after dialysis were decreased significantly compared to before dialysis. Type of membrane (high flux vs. low flux) had not significant effect in PFT results of the patients ($P>0.05$).
Conclusion: Since high flux membranes are more expensive than low flux membranes and there was no significant difference in the results of spirometry of patients, it could not be offered the use of high flux membrane for this purpose.

P3209

Pulmonary volumetric analyses based on three-dimensional computed tomography (3D-CT), compared with pulmonary function test

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Background: Three-dimensional computed tomography (3D-CT) potentiates the application to the daily clinical practice.
Methods: Forty four patients (30 COPD, 12 lung cancer, 2 miscellaneous) were enrolled in this study. Lung volumes (LV), as well as the low attenuation volume (LAV), were measured based on 3D-CT both at the end inspiratory volume (EIV) and at the end expiratory volume (EEV) and compared with the physiological data of ordinary pulmonary function tests.
Results & discussion: Lung volumes determined using reconstituted 3D-CT images at end inspiratory volume (LVins), those at end expiratory volume (LVexp), and their difference (LVins – LVexp), were significantly associated with TLC ($p<0.0001$), RV ($p<0.0001$), VC ($p=0.0028$), respectively. Furthermore, the percentage of the LAV to LV at EIV (LAV%ins) was associated with the changes in the various results of pulmonary function tests, including FEV1, %FEV1, RV/TLC, VC. Both FEV1 and %FEV1 were associated with LAVexp and LVexp, in participants whose LAV were larger than 10mL. These results suggested that 3D-CT, taken at both EIV and EEV, provides the data not only on lung volumes in the static state, but also dynamic infomation. Furthermore, there is a significant association between the FEV1 and the difference between the normal attenuation volumes (NAV) of the 3D-CT at EIV and those at EEV ($p<.001$). This suggested that not only LAV but also NAV contributed to the airflow limitation, represented by FEV1 reduction.
Conclusion: 3D-CT reveals not only the physiologic properties, but also provides some insights into the mechanism of respiration.

P3210

A new ultrasonographic device for within-breath measurements of diaphragm thickness during breathing

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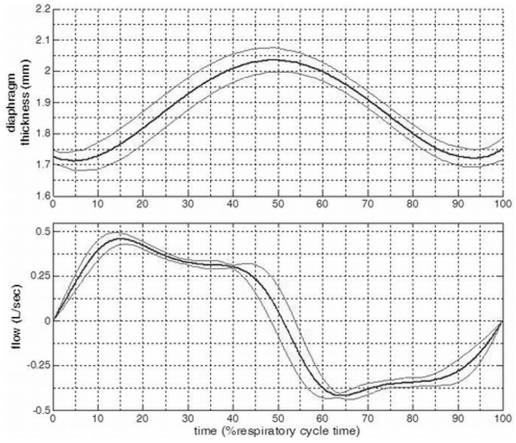
Preliminary studies have shown the possibility to use ultrasounds (US) to measure diaphragmatic thickness (DT). In order to allow accurate and operator-free US measurements of within-breath DT during tidal breathing, we have designed and prototyped an innovative US device composed by a single piezo-element probe (SPEP, 7.5 MHz) able to generate and detect radio frequency (RF) echo signals of the pleural and peritoneal membranes of the diaphragm. The prototype was tested on a phantom and successively on 6 healthy subjects (3M, 3F), who were studied in supine position during spontaneous quiet breathing at rest. The SPEP was fixed by adhesive tape on the lateral ribcage (9th or 10th intercostal space) and data were acquired continuously and synchronously with a pneumotachograph. The in-vitro validation showed an accuracy of ±0.05 mm. In average, DT thickness was 1.55±0.17 and 1.9±0.21 mm, respectively at end-expiration and end-inspiration. DT variations during tidal breathing were in average 0.35±0.05 mm with different patterns of within-breath DT changes (see figure for a representative example).
In conclusion, the SPEP device: a) is characterized by measurement accuracy able



to detect the small changes of DT during quiet breathing; b) allows an operator-free method to monitor DT during breathing and to study different patterns of DT variations, corresponding to different timing of diaphragm activation.

P3211

Estimation of chest-wall mechanics by laser self mixing interferometer

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Background: Several studies demonstrated that the chest wall (CW) may be split into at least two compartments (rib cage and abdomen) characterized by spatial distribution inhomogeneities in CW mechanics. Up to now, it has been assessed by means of complex technique such as Optoelectronic Plethysmography (OEP). We have developed a CW scanning system (CWSS) based on self-mixing laser interferometers that allows measuring relative displacement contactless with high spatial resolution (<1 μm) in an economical and easy to use way.
Methods: Five healthy subjects, in supine position, were analyzed while submitted to a sinusoidal pressure forcing at the mouth with components at 5, 11 and 19 Hz. Displacement of several points on their CW has been measured with the CWSS and phase shift among these points and the pressure stimulus was estimated by spectral analysis.
Results: The impedance averaged maps in the figure below show high spatial inhomogeneities, in particular one may appreciate that at 5 Hz it is possible to identify the region of the rib cage, where the pressure stimulus moves fast, and the abdomen where the pressure wave is slowed down by the high inertive component.

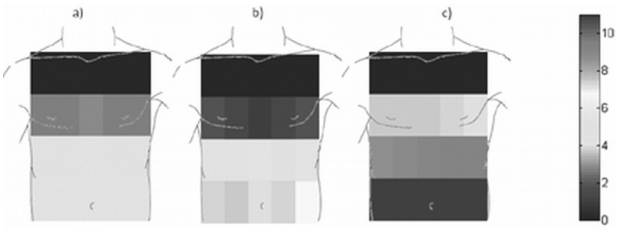

Figure. Panel a) phase shift at 5 Hz, panel b) phase shift at 11 Hz, panel c) phase shift at 19 hz

This trend tends to be less marked as the frequency increased, indeed at 19 Hz, we can still see heterogeneity, but the phase shift tends to get similar to a line. In the figure the phase shift color map is reported.

P3212

Specificity and sensitivity of the methacholine challenge test for the diagnosis of asthma in athletes

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The report of recurrent symptoms of bronchial obstruction as chest tightness, wheeze and cough provoked by exercise is a prerequisite for the diagnosis of asthma or exercise-induced bronchospasm (EIB) in athletes. The report of symptoms should be verified by the demonstration of reversibility of airflow obstruction, EIB or other methods of diagnosing either indirect or direct bronchial hyperresponsiveness (BHR). The purpose of this study was to examine specificity and sensitivity of the methacholine challenge test (MCT) for the diagnosis of asthma in athletes.
Twenty seven athletes (16 M/11 F, mean age 22.0±4.3 yrs) with respiratory

symptoms were studied. Lung function with assessment of reversibility to salbutamol (n=27) and challenge tests with methacholine (n=25) were performed. The specificity and sensitivity of the MCT were evaluated.
Significant reversibility to salbutamol was found in 7 athletes. The fall in forced expiratory volume in one second (FEV1) following the methacholine inhalation (≤8 mg/ml) was more than 20% in 16 athletes (30.0±9.6% vs 12.3±7.1% in nonresponders (n=9), p<0.0001). The MCT-BHR test showed high specificity (100%), but a lower sensitivity (80%) and negative predictive value (55.6%). At the moderate BHR cutoff value (≤ 4 mg/ml), the MCT-BHR test had a more low sensitivity (70%) and negative predictive value (45.5%).
Assessment of bronchial responsiveness by a direct method (bronchial provocation with methacholine) is a good procedure of diagnosing asthma in athletes. The MCT-BHR test in athletes with respiratory symptoms had a high specificity and sensitivity and cutoff value for high BHR may be more useful.

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Bronchial hyper-reactivity diagnosed by methacoline challenge and the pre-test clinical probability

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Aim: To assess the correlation between methacoline challenge results and the pre-test clinical probability of bronchial hyper-reactivity.
Subjects and methods: Patients with respiratory symptoms raising suspicion of asthma and patients with partially controlled asthma performed methacoline challenge (MC) using ATS Guidelines (1999). The test was considered negative for a PC20 >16 mg/mL and borderline for 8-16 mg/mL. Bronchial hyper-reactivity was considered severe for PC20 <0.125 mg/mL.
Pre-test probability of bronchial hyper-reactivity was recorded by the pulmonologists using visual analogic scale (VAS) based on history, clinical findings and previous spirometry results; the scores ranged from 0 (no hyper-reactivity) to 10 (doubtless hyper-reactivity).
Results: 50 patients were evaluated. VAS scores and PC20 values differed significantly in the two groups:
– In the 26 patients with known asthma VAS scores were 5.1-10 (mean 7.6). MC showed moderate or severe bronchial hyper-reactivity in all subjects, with PC20 0.03-2 mg/mL (mean 0.56).
– In the 24 patients with suspicion of asthma VAS scores were 0.9-9 (mean 4.8). MC was negative in 13, borderline in 2 patients and showed bronchial hyper-reactivity in 9 (severe in 1, moderate in 5, mild in 3 patients; mean PC20 5.3).
A strong correlation was seen between VAS pre-test scores and PC20 values in the suspicion of asthma group (r=-0.832, p=0.000) and a weak correlation in the known asthma group (r=-0.389, p=0.049).
Conclusions: Pre-test clinical probability of bronchial hyper-reactivity recorded by the pulmonologists on visual analogic scale correlated well with the PC20 values at methacoline challenge in patients with suspicion of asthma.